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10/650,326	08/28/2003	Keith A. Hruska	JJJ-P01-599	6882

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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	**PAPER NUMBER**
1649	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/650,326	HRUSKA ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56,69-76 and 78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56,69-76 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *26 March 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

The amendment filed 26 March 2007 is acknowledged. Claims 56 and 78 are cancelled. Claims 1-6, 12-17, 57 and 77 are cancelled. Claims 56, 69-76 and 78 are under examination.

Objections Withdrawn

Claim Objections

The objection to claim 78 for informalities is withdrawn in response to Applicants' amendment of the claim to read "A packaged pharmaceutical comprising..."

Information Disclosure Statement

The objection to the information disclosure statement (IDS) filed 9 February 2006 because the reference (AG) listed as U.S. Patent No. 5,733,441 (Higley et al.) is by Chi Yin-Ko and pertains to a pre-wet filter system is withdrawn in response to Applicants' submission of a supplemental IDS on 26 March 2007 with the correct patent number.

Rejections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 56 and 70-76 and 78 under 35 U.S.C. 103(a) as being unpatentable over Sampath et al. (U.S. Patent No: 6,498,142, filed 6 May 1996) in view of London et al. (Journal of hypertension. 1996; 14: 1139-46) is maintained for reasons of record as set forth at pages 4-6 of the Office action mailed 21 September 2006.

Applicants argue at p. 6, 3rd and 4th full paragraphs that Applicants have disclosed unexpectedly superior properties of the claimed compositions over a spectrum of properties, for example, the combination of OP-1 and enalapril is far superior in treating proteinuria than either component alone (see p. 143, lines 6-10). This argument has been fully considered, but is not found persuasive because the showing should demonstrate that synergism is unexpected. See *In re Huellmantel*, 324 F.2d 998, 139 USPQ 496 (CCPA 1963); *In re Meinhardt*, 392 F.2d 273, 157 USPQ 270 (CCPA 1968). A greater than additive effect is not necessarily sufficient to overcome a

prima facie case of obviousness because such an effect can either be expected or unexpected. Applicants must further show that the results were greater than those which would have been expected from the prior art to an unobvious extent. Ex parte The NutraSweet Co., 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991) (Evidence showing greater than additive sweetness resulting from the claimed mixture of saccharin and L-aspartyl-L-phenylalanine was not sufficient to outweigh the evidence of obviousness because the teachings of the prior art lead to a general expectation of greater than additive sweetening effects when using mixtures of synthetic sweeteners). See MPEP 716.02(A) [R-2]. In other words "synergism" is ***not*** "per se" unexpected. Note that the argument at p. 7 regarding the unexpected improvement of the combined treatment of OP-1 and enalapril in the treatment of glomerular filtration rate (GFR) is not relevant to claims 56, 70-76 and 78 since those claims are not limited to enalapril, and the unexpected results (no effect with enalapril, improvement with OP-1 and even greater improvement with OP-1 and enalapril combination treatment) have not been tested for other ACE inhibitors, thus the evidence is not commensurate in scope with Applicants' claims

The combined teachings of Sampath et al. and London et al. suggest that OP-1 and ACE inhibitors, respectively, are useful in the treatment of renal disease. The person of ordinary skill in the art would have been motivated to co-treat with ACE inhibitors because renal disease is known to be complicated with hypertension and it is known that hypertension must be controlled in renal disease (see abstract of London et al.). Furthermore, the person of ordinary skill in the art could have reasonably expected

success because both compositions are known in the art for treating renal disease, so the combining the compositions in one packaged pharmaceutical would have a reasonable expectation of success. Thus the claims do not contribute anything non-obvious over the prior art.

The rejection of claims 56 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sampath et al. (U.S. Patent No: 6,498,142) in view of London et al. (Journal of hypertension. 1996; 14: 1139-46) as applied to claims 56 and 70-76 and 78 in the immediately preceding paragraph and further in view of Salvetti (Drugs. 1990; 40: 800-28).

Applicants argue p. 7 regarding there is an unexpected improvement of the combined treatment of OP-1 and enalapril in the treatment of GFR. Specifically, the results show no effect on GFR with enalapril, some improvement of GFR with OP-1 and even greater improvement of GFR with OP-1 and enalapril combination treatment.

This argument has been fully considered but is not found persuasive for the following reasons. Although Applicants suggest why synergism may be unexpected (there was no effect on GFR with enalapril alone), the prior art suggests that enalapril administration would improve GFR. For instance, Reams et al. (J Clin Hypertens. 1986; 2: 55-63), teach that enalapril improves GFR in patients whose renal function was impaired from hypertension (see abstract). Reams also teaches at p. 62, 1st paragraph that "[gains] in glomerular filtration rate and effective renal plasma flow were achieved without adverse effect on 24-hour urinary protein excretion; indeed, most patients

demonstrated a decrease in protein excretion.", thus the art suggests both GFR and proteinuria were improved. In addition, Mahajan et al. (J Assoc Physicians India. 1996; 44: 323-4) teach that enalapril increases renal blood flow, thus improves GFR (see abstract; p. 324, last paragraph). Given that there is guidance in the to the effect that enalapril improves GFR, the assertion of unexpected results is not persuasive.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 56, 71-76 and 78 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,677,432 in view of in view of London et al. (cited above) and further in view

of Vukicevic et al (J Clin Invest. 102; 1998: 202-214) is maintained for reasons of record as set forth at pages 8-10 of the Office action (mailed 21 September 2006).

Applicants state at p. 8, 3rd paragraph that they will consider filing a suitable disclaimer upon notification of allowable subject matter. As no allowable subject matter has yet been indicated, the rejection is maintained.

The rejection of claims 56 and 69 are on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,677,432 in view of in view of London et al. (cited above) as applied to claims 56, 71-76 and 78 in the immediately preceding paragraphs and further in view of Vukicevic et al. and Salvetti (both cited above) is maintained for reasons of record as set for the at pages 11-12 of the previous Office action (mailed 21 September 2006).

Applicants state at p. 8, 3rd paragraph that they will consider filing a suitable disclaimer upon notification of allowable subject matter. As no allowable subject matter has yet been indicated, the rejection is maintained.

The rejection of claims 56, 71-76 and 78 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,846,906 in view of in view of London et al. (Journal of hypertension. 1996; 14: 1139-46) and further in view of and further in view of Vukicevic et al (J Clin Invest. 102; 1998: 202-214) as set forth at pages 13-14 of the of the previous Office action (mailed 21 September 2006).

Applicants state at p. 8, 3rd paragraph that they will consider filing a suitable disclaimer upon notification of allowable subject matter. As no allowable subject matter has yet been indicated, the rejection is maintained.

The rejection of claims 56 and 69 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,846,906 in view of in view of London et al. (cited above) as applied to claims 56, 71-76 and 78 in the immediately preceding paragraphs and further in view of Vukicevic et al. and Salvetti (both cited above) as set forth at p. 14 of the previous Office action (mailed 21 September 2006) is maintained for reasons of record.

Applicants state at p. 8, 3rd paragraph that they will consider filing a suitable disclaimer upon notification of allowable subject matter. As no allowable subject matter has yet been indicated, the rejection is maintained.

The provisional rejection of claims 56, 71-76 and 78 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 16-18 of copending Application No. 10/816,768 in view of in view of London et al. (Journal of hypertension. 1996; 14: 1139-46) and further in view of and further in view of Vukicevic et al (cited above) as set forth at pages 15-16 of the previous Office action (mailed 21 September 2006) is maintained for reasons of record.

Applicants argue at p. 8, last paragraph that a provisional double patenting rejection should be dropped if it is the only one remaining in the application (see MPEP 804). Since other rejections remain of record, the provisional application is maintained.

The provisional rejection of claims 56 and 69 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 16-18 of copending Application No. 10/816,768 in view of in view of London et al. (cited above) as applied to claims 56, 71-76 and 78 in the immediately preceding paragraphs and further in view of Vukicevic et al. and Salvetti (both cited above) as set forth at pages 16-17 of the previous Office action (mailed 21 September 2006) is maintained for reasons of record.

Applicants argue at p. 8, last paragraph that a provisional double patenting rejection should be dropped if it is the only one remaining in the application (see MPEP 804). Since other rejections remain of record, the provisional application is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest, Ph.D.

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646